REMARKS

Claims 1-6 and 8-77 are pending in the present application. Among them, Claims 48-81 are directed to non-elected inventions and are withdrawn from further consideration. Applicants will cancel these claims as appropriate upon indication of allowable subject matter.

Applicants note that the IDS received on August 11, 2006 has been considered by the Examiner.

Applicants respectfully request reconsideration in view of the following remarks. Issues raised by the Examiner will be addressed below in the order they appear in the Office Action.

Claim rejections under 35 U.S.C. § 112, second paragraph

Claims 1-6 and 8-47 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Office Action argues that "... while the claim is drawn to a method, there are still no actual method steps beyond merely 'culturing.' ... The claims do not set forth how the cells are cultured or when or why one moves from culturing step to culturing step (claim 41) and thus the metes and bounds of the invention are not clearly set forth."

Applicants first note that only independent Claim 1 and its dependent Claims 2-14 appear to fit the reason for rejection (*i.e.*, "no actual method steps beyond merely 'culturing'"), since independent Claims 15 and 41 contain other steps including at least the "dissociating" step (c) and the "plating" step (e).

Second, Applicants submit that "culturing" is a method step that adequately delineates the metes and bounds of the invention intended to be claimed.

Pursuant to MPEP 2173.04: "[b]readth of a claim is not to be equated with indefiniteness. *In re Miller*, 441 F.2d 689, 169 USPQ 597 (CCPA 1971). If the scope of the subject matter embraced by the claims is clear, and if applicants have not otherwise indicated that they intend the invention

to be of a scope different from that defined in the claims, then the claims comply with 35 U.S.C. 112, second paragraph."

Here, with respect to method Claims 1-14, all that is required is a single "culturing" step. Applicants submit that there is no requirement to have multiple steps in a method claim. Nor is there a requirement for the step(s) to set forth how the cells are cultured or when one moves from culturing step to culturing step, because it is the specification, not the claims, that teaches one of skill in the art how to make and use / practice the claimed invention. In addition, regarding why one moves from culturing step to culturing step, Applicants submit that there is no requirement for Applicants to explain how or why the claimed invention works. *Parker v. Frilette*, 462 F.2d 544, 547, 174 USPQ 321, 324 (CCPA 1972) ("[an] inventor need not understand precisely why his invention works in order to achieve an actual reduction to practice"). MPEP 2138.05.

Claims 15-40 are allegedly rendered indefinite by the phrase "bioactive fragment thereof." The Office Action argues that "it is unclear which activity or fragments the claim refers."

Applicants submit that a skilled artisan would understand that "activity" unambiguously refers to relevant biological activities of the recited FGF polypeptides. For example, if FGF-8 is used in method step (c) in Claim 15, a "bioactive fragment thereof" includes a FGF-8 fragment that lacks part of the wild-type FGF-8 amino acid sequence, but nevertheless is still "bioactive" for the purpose of carrying out steps (c) and/or (d) in place of the wild-type FGF-8. Thus a skilled artisan would understand that any such fragments of the recited FGF polypeptides, so long as they can be used to carry out the relevant step(s) like the recited FGF polypeptides, are within the scope of the claim.

The Office Action also states that "[t]he claims would more accurately define applicant's invention if the cells were phenotypically defined (at least the cell type) beyond just insulin." Applicants take this as a suggestion by the Examiner to improve claim language. Applicants do appreciate the Examiner's suggestion, but prefer not to amend the claims at this stage because Applicants believe that the current claim language adequately defines what Applicants intend to claim.

In view of the foregoing, Applicants submit that all claims satisfy the requirement of 35 U.S.C. § 112, second paragraph. Reconsideration and withdrawal of the rejections are respectfully requested.

Claim rejections under 35 U.S.C. § 112, first paragraph – Written Description

Claims 15-40 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the invention(s), at the time the application was filed, had possession of the claimed invention.

Specifically, the Office Action argues that the specification does not contain an adequate description for the entire scope of the claim with respect to the genus of "polypeptide being at least 60% identical to" or "bioactive fragment of" certain FGFs.

Applicants have amended Claim 15 to clarify the subject matter claimed. Support can be found throughout the specification. *See*, for example, paragraph **[0116]** of the published application US 2004-0110287 A1. Applicants submit that at least the claims as amended satisfy the written description requirement.

Applicants wish to draw the Examiner's attention to a recent PTO Board decision, which supports Applicants' position that the specification provides adequate written description for the recited genus of FGF polypeptides and bioactive fragments in the amended claims. *See Ex parte Bandman*, No. 2004-2319, (BPAI 2005).

In *Bandman* (U.S. Application No. 09/915,694), Applicants appealed a Final rejection by the Examiner, and the Board reversed the rejections based on both the written description and enablement requirements of 35 U.S.C. § 112, first paragraph to one of the claims on appeal. Pointedly, the Board found that claims directed to a naturally occurring amino acid (or polynucleotide) sequence at least 95% identical to the disclosed amino acid (or polynucleotide) sequence were enabled and met the written description requirement, even in the absence of explicitly reciting a *functional requirement* of the claimed sequences.

Claims 3 of the '694 application, which was representative of the subject matter on appeal, recites, *inter alia*, "an isolated polynucleotide encoding a polypeptide comprising a naturally occurring amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 1 (Claim 3)." The Examiner rejected this claim for allegedly failing to comply with the written description requirement, asserting that the specification provides only a single representative species – the polynucleotide of SEQ ID NO: 2 (which encodes the amino acid sequence of SEQ ID NO: 1), and fails to disclose any structure-function relationship in this species.

The Board reversed the written description rejection, noting that "[t]he written description requirement . . . does not require a description of the complete structure of every species within a chemical genus." *Bandman*, No. 2004-2319 at p. 3. The Board also compared the circumstances of *Bandman* with those faced by the Federal Circuit in *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 296 F.3d 1316 (Fed. Cir. 2002). In *Enzo Biochem*, the Federal Circuit determined that an "[a]dequate written description may be present for a genus of nucleic acids based on their hybridization properties, 'if they hybridize under highly stringent conditions to known sequences because such conditions dictate that all species within the genus will be structurally similar.'" (citing *Enzo Biochem*, 296 F.3d at 1324). Thus in *Bandman*, the Board determined that the genus of molecules defined by the claims was similarly limited, and reversed the Examiner's written description rejection.

Applicants submit that the fact pattern of *Bandman* is essentially identical to the instant application, and thus *Bandman* should apply. Applicants note that in *Bandman*, Claim 3 does not even recite a biological function of the claimed genus of polypeptides and polynucleotides. Nevertheless, the Board found that the limitation "naturally occurring sequences" implicitly requires that these claimed sequences to be functional (*i.e.*, having retained malate dehydrogenase activity). In the instant case, Claim 15 explicitly recites "FGF polypeptide ... or bioactive fragment thereof," thus the claim at least implicitly requires the FGF polypeptides or fragments thereof to be bioactive, *i.e.*, having a bioactivity shared with the parent FGF polypeptide. Furthermore, the *Bandman* claim is directed to a composition of matter, while the claimed invention here is a method. In order for the claimed method to work, the FGF polypeptide or fragment used therein must, by definition, be functional, or the method steps using these polypeptides will be rendered meaningless. This would

be immediately recognized by one of skill in the art. Therefore, Applicants submit that the claimed subject matter is even more thoroughly described than that in *Bandman*.

For example, regarding describing "a representative number of species by actual reduction to practice," *Bandman* only describes a *single* novel sequence (species) within the claimed genus. There were no other known species within the genus. Here, in contrast, a great many well-characterized FGF polypeptides species are disclosed in the instant specification and/or known in the art (*see*, for example, paragraph [**0113**] of the published specification US 2004-0110287 A1, referring to "20 identified mammalian FGFs").

Indeed, pursuant to MPEP 2163, "[t]he written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice ..., reduction to drawings ..., or by disclosure of relevant, identifying characteristics, *i.e.*, structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus ... *See Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406."

"The description need only describe in detail that which is new or not conventional. ... What is conventional or well known to one of ordinary skill in the art need not be disclosed in detail." *See, e.g., Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986). "If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met. *See, e.g., Vas-Cath*, 935 F.2d at 1563, 19 USPQ2d at 1116; *Martin v. Johnson*, 454 F.2d 746, 751, 172 USPQ 391, 395 (CCPA 1972)." MPEP 2163.

Therefore, with respect to the recited FGF polypeptide genus, a large number of species representative of the entire genus had been reduced to practice and were generally known in the art at the time the present application was filed, and what is well known to one of ordinary skill in the art need not be described in detail. With regard to FGF polypeptides, one of skill in the art would have readily understood the inventor to be in possession of these peptides as recited in the pending

claims. This alone provides adequate written description for the recited FGF polypeptide genus.

Furthermore, regarding describing "relevant, identifying characteristics" of the recited genus, no relationships between structure and function were known to those of skill in the art in *Bandman*. In the instant recited genus, there is an art-recognized conserved functional domain for FGF polypeptides. Because of the presence of this simple yet conserved structure, the known FGF polypeptides constitute representative species of the entire genus, such that a person of ordinary skill in the art could immediately envisage the entire genus of FGF polypeptides and bioactive fragments thereof in view of the disclosure in the specification and the knowledge in the art.

In summary, one of skill in the art encountering the term "FGF polypeptide" has the benefit of substantial background knowledge regarding such peptides, their structure, their function, and the structural and functional characteristics recited in the claim provide additional clarification of the scope and meaning of this claim element. Thus, if the Board held that a single novel sequence in *Bandman* is representative of the claimed genus (and satisfies the written description requirement), then it seems only logical to conclude that a wealth of known species ought to be representative of a similarly recited genus.

Regarding "bioactive fragment thereof," Applicants submit that the recited FGF polypeptides are all small growth factors with about 200 amino acids (or about 20-25 kDa). As a skilled artisan will appreciate, these recited FGF polypeptides share an even smaller highly conserved 120-amino acid core (about 13 kDa) towards the middle of the polypeptides. Thus it is probable that all bioactive fragments contain this small but highly conserved core domain. In other words, all "bioactive fragments thereof" are not expected to be very different from the known core sequences of the known FGF polypeptides, and can be adequately represented by these core sequences.

Therefore, the claims as amended recite a genus of FGF polypeptides that are adequately represented by the known FGFs disclosed in the specification and generally known in the art. Applicants' position is supported by MPEP 2163 and the Board decision in *Ex parte Bandman*. Thus, all pending claims meet the requirement of 35 U.S.C. § 112, first paragraph. Reconsideration and withdrawal of the rejections are respectfully requested.

CONCLUSIONS

In view of the above amendment, applicant believes the pending application is in condition for allowance. Applicant believes no fee is due with this response. However, if a fee is due, please charge our Deposit Account No. **18-1945**, from which the undersigned is authorized to draw under Order No. **ESCL-P01-124**.

Dated: May 29, 2007

Respectfully submitted,

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